Appl. No. Filed

09/492,709

January 27, 2000

expressing an antisense nucleic acid against a nucleic acid encoding said gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell;

contacting said sensitized cell with a candidate compound; and

determining whether said candidate compound inhibits the growth of said sensitized cell to a greater extent than said candidate compound inhibits the growth of a nonsensitized cell.

- 38. (Amended) The method of Claim 36, wherein said cell is from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella cholerasuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, *and Chlamydia trachomatus*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.
- 68. (Amended) A method of screening a candidate compound for the ability to inhibit proliferation of a microorganism said method comprising:
 - (a) identifying a gene or gene product required for proliferation in a first microorganism;
 - (b) identifying a homolog of said gene or gene product in a second microorganism;
 - (c) identifying an inhibitory nucleic acid sequence which inhibits the activity of said homolog in said second microorganism;
 - (d) contacting said second microorganism with a proliferation-inhibiting amount of said inhibitory nucleic acid, thus sensitizing said second microorganism;
 - (e) contacting the sensitized microorganism of step (d) with a candidate compound; and

Appl. No. Filed

09/492,709

ed : January 27, 2000

(f) determining whether said candidate compound inhibits proliferation of said sensitized microorganism to a greater extent than said candidate compound inhibits proliferation of a nonsensitized microorganism.

- 79. (Amended) A method of screening a candidate compound for the ability to inhibit proliferation said method comprising:
 - (a) identifying an inhibitory nucleic acid sequence which inhibits the activity of a gene or gene product required for proliferation in a first microorganism;
 - (b) contacting a second microorganism with a proliferation-inhibiting amount of said inhibitory nucleic acid, thus sensitizing said second microorganism;
 - (c) contacting the proliferation-inhibited microorganism of step (b) with a candidate compound; and
- (d) determining whether said candidate compound inhibits proliferation of said sensitized second microorganism to a greater extent than said candidate compound inhibits proliferation of a nonsensitized second microorganism.
- 85. (Amended) A method of screening a candidate compound for activity against a biological pathway required for proliferation, wherein said candidate compound is not previously known to possess the ability to reduce proliferation, said method comprising:

sensitizing a cell by expressing an antisense nucleic acid against a nucleic acid encoding a gene product required for proliferation in a cell to reduce the activity or amount of said gene product;

contacting the sensitized cell with a candidate compound; and

determining whether said candidate compound inhibits the growth of said sensitized cell to a greater extent than said candidate compound inhibits the growth of an nonsensitized cell.

88. (Amended) The method of Claim 85, wherein said cell is from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*. *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella cholerasuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus*

Appl. No.

09/492,709

Filed

January 27, 2000

anthracis, Yersinia pestis, Clostridium botulinum, Campylobacter jejuni, and Chlamydia trachomatus, Chlamydia pneumoniae or any species falling within the genera of any of the above species.

96. (Amended) A method of screening a candidate compound for the ability to inhibit cellular proliferation, wherein said candidate compound is not previously known to possess the ability to inhibit cellular proliferation, said method comprising:

contacting a cell with an agent which reduces the activity or level of a gene product required for proliferation of said cell;

contacting said cell with a candidate compound; and

determining whether said candidate compound reduces proliferation to a greater extent than said candidate compound reduces proliferation of a cell which has not been contacted with said agent.

- 111. (New) The method of Claim 99, wherein said agent is an antisense nucleic acid directed to a gene or operon required for proliferation.
- 112. (New) The method of Claim 68, wherein said candidate compound is a compound not previously known to possess the ability to inhibit cellular proliferation.
- 113. (New) The method of Claim 79, wherein said candidate compound is a compound not previously known to possess the ability to inhibit cellular proliferation.
- 114. (New) The method of Claim 35, wherein said candidate compound is present in a natural product extract.
- 115. (New) The method of Claim 68, wherein said candidate compound is present in a natural product extract.
- 116. (New) The method of Claim 79, wherein said candidate compound is present in a natural product extract.
- 117. (New) The method of Claim 85, wherein said candidate compound is present in a natural product extract.
- 118. (New) The method of Claim 96, wherein said candidate compound is present in a natural product extract.